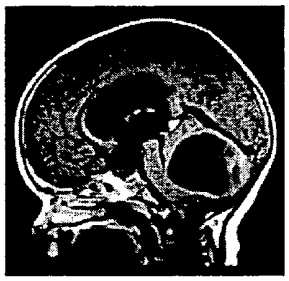

The University of Oklahoma

Health Sciences Center

DEPARTMENT OF NEUROSURGERY

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Annex-5

Research:

For a list of recently published abstracts, go here

Current Research Projects in the Department Laboratories

- Relationship Between Spinal Motion and Neurologic Deficit in Cervical Spondylotic Myelopathy
  - Cervical spondylotic myelopathy (CSM) is a common condition i which there is narrowing of the spinal canal in the neck, usually c arthritis, multiple herniated discs, or bone spurs. As a result, patie begin losing movement and feeling in their arms and legs. Variou treatments are performed for this problem, the most common of v is surgery. Multiple surgical options are currently available, thou address different aspects of the problem. Unfortunately, treatmen

failures are common.
Treatment of patients with CSM could potentially be improved b
better understanding of the disease process. Though we know tha
cervical spinal canal is narrowed in CSM, we do not know how t
causes loss of movement and feeling. Laboratory experiments ha
shown that more spinal cord compression is required to recreate
than is usually present in the patients that come to surgery. This
suggests that there may be some other important factor involved.
In addition to the spinal cord compression present at rest, we kno
the spinal cord is stretched and further compressed each time the
is moved. Though long term experiments have shown that this
movement may be important, no detailed experiments have been
to investigate this.
The purpose of this project is to determine the relationship betwe
spinal motion and the neurological deficits (weakness and loss of
feeling) seen in CSM. In order to do this, we plan to recreate the
canal narrowing seen in the human condition in the cat cervical s
Using the information obtained during the experiment, we will be
to determine how important spinal motion is in producing the we
and loss of feeling seen in CSM. This information, in turn, will h
decide with some objectivity what the best treatment is for our pa
Research done under the direction of Christopher E.Wolfla, M.D.

- The Involvement of Bradykinin in the Pathology of Cerebral T
  - Bradykinin is a member of the family of peptide hormones know
    kinins having a variety of physiological and pathophysiological e
    Bradykinin is recognized as a potent stimulator of pain and is ger
    in response to cellular injury. In addition, bradykinin is a potent
    vasodilator. The presence of a kinin system in the **brain** has been
    established. It is proposed that the kinins and bradykinin, in parti
    play an important role in the cerebrovascular pathophysiology re
    from cerebral trauma. The project will investigate the role of
    bradykinin in a fluid percussion head cerebral trauma model. Usi
    closed cranial window, cerebral pial vessel diameter will be moni
    continuously during fluid percussion of injury. Impact pressure w
    varied. Specific antagonists to bradykinin will be used to attenuat
    vasodilatory effect. Continuing studies will evaluate the involven
    systems activated by bradykinin, i.e. arachidonic acid cascade,
    excitatory amino acids, nitric oxide, in the pathophysiology of he
    injury. Techniques used in the project include laser Doppler flow
    closed cranial window, and PC based video imaging with
    morphometric measurement of vessel diameter. Research done u
    the direction of Paul C. Francel, M.D., Ph.D..

- Conduit Assisted Regeneration of Peripheral Nerves
  - Long nerve gaps continue to a difficult problem for the periphera
    nerve surgeon. The present gold standard is an interposed nerve
    autograft placed to assure the anatomic integrity of the proximal
    to the distal degenerating nerve. The regenerating nerves progres
    along the nerve graft scaffold and into the remains of the distal n

reinnervate the distal motor end plates or sensory organs. The is accomplished at the cost of potential donor site complications inc numbness, painful neuroma formation and unacceptable scarring. Conduit repairs have been attempted to avoid these donor complications. The conduits used have included synthetic materi autologous artery and vein, and muscle. To date no satisfactory c has been found. Previous work by Dr. Francel has documented th utility of a silastic conduit in promoting sciatic nerve growth ove up to 1.5cm, a distance that precludes non-assisted regeneration. project will evaluate the utility of a commercially available, bioresorbable material for use as a conduit in the sciatic nerve inj model. The project will evaluate groups including no implant, autologous nerve implant, silastic conduit implant and bioresorba implant. In addition to the potential value in peripheral nerve regeneration, these studies will supply information useful in assis regeneration of central nervous system tissues. Techniques involv include peripheral nerve surgery, lesion generation, conduit implantation, tissue harvest, and tissue preparation for histologic evaluation of nerve regeneration. Research done under the directi Paul C. Francel, M.D., Ph.D..

- Shunt Valve Function in Relation to Placement
  - A variety of shunt valve systems have been devised with siphon-control (SCD) devices designed to prevent overdrainage of cerebrospinal fluid. To date, no compelling evidence has been presented to document the utility of these devices. Estimates of overdrainage are reported in the range of 30%. When reviewing t product literature with regard to surgical placement of these devi there is a recommendation that the valve- SCD assemble be place the level of the inlet catheter tip. Placement above this level will in higher intra-ventricular pressures and slower than specified ou rates, and placement of the assemble below this level will result i lower intra-ventricular pressures with higher than specified outfl rates. It is our proposal that valve placement with regard to inlet catheter tip is absolutely essential for proper function of the valv project will evaluate, on the bench, a variety of shunt valve types a number of manufacturers. Valves will be positioned such that t are flowing at a nominal rate of 50ml/hr by adjusting the starting pressure. Lower resistance valves will require a lower head press attain this flow rate. The position of the inlet catheter tip will be at this 0 level, and the valve-SCD will be moved in relation to the tip. Both positive and negative offsets will be used. Preliminary evidence has shown that elevating the valve-SCD above the inlet results in a significant reduction of outflow. Movement of the val below the level of the inlet tip results in significant increases in o rate. The changes in outflow rate are proportional to the distance between the valve assembly and the inlet catheter tip. The net eff moving the valve with respect to the inlet tip is to alter the head pressure on the inlet side of the valve, thereby controlling flow in pressure dependent fashion. Research done under the direction of C. Francel, M.D., Ph.D..

- Delivery of **Doxorubicin** (Adriamycin) to the **Brain** for Treatn of Tumors
  - **Doxorubicin** is an effective chemotherapeutic drug for breast car Since 17% of all breast cancer patients experience metastases to t **brain, doxorubicin** could be potentially useful in the treatment o these tumors. However, **doxorubicin**, even in low dose, is highly neurotoxic, precluding it's use for tumors of this nature. Recent development of drug encapsulation in sterically stabilized liposor (Stealth Liposomes) offers hope of avoiding high tissue levels of drug to attain therapeutic concentrations. The liposomes serve as second compartment for the drug, releasing it slowly to the tissue significantly increasing the plasma and tissue half-life of the drug Although penetration of **doxorubicin** and liposome encapsulated **doxorubicin** into the **brain** is prevented by the intact blood-**brai** barrier, we have been using hyperosmotic blood-**brain** barrier disruption to effect delivery of normally excluded agents to the **b** parenchyma. This study is designed to investigate the penetration distribution of both free and liposomal encapsulated **doxorubicin** normal **brain** following blood-**brain** barrier disruption. The continuation of these studies involves determination of the kineti **doxorubicin** in **brain** and evaluation of the neurotoxicity of the encapsulated drug. Techniques include blood-**brain** barrier disru and scanning confocal laser microfluorometry for detection of **doxorubicin** autofluorescence. Research done under the directio Mary K. Gumerlock, M.D.

Current Clinical Research Projects

- BBBD - Blood **Brain** Barrier Disruption Study
  - This study has four specific aims:
    - To evaluate the efficacy between post-operative focal crani irradiation followed by combination chemotherapy (intraar methotrexate and intravenous cytoxan) with BBBD (Arm I postoperative combination chemotherapy (intraarterial methotrexate and intravenous cytoxan) with BBBD follow focal cranial radiation (Arm II)
    - The second goal is to evaluate differences in tumor respons any, between patients in Arm I and Arm II.
    - The third goal is to assess patient clinical and cognitive fur and evaluate and compare treatment related neurotoxicity, in each ARM and between the ARMS through serial neuropsychologic testing and radiographic imaging.
    - The fourth goal is to prospectively evaluate the differences response, survival, and function, if any, between patients undergoing initial tumor diagnosis by biopsy or surgical resection.

- BAK/C Interbody Fusion Study
  - The purpose of this study is to determine the safety and effectivei the BAK/C Interbody Systen as compared to an uninstrumented / (anterior cervical discectomy with fusion) for one and two level disease. Patients fitting inclusion criteria will be randomized into groups. The three groups are BAK/C, BAK/C with a hydroxyape coating, and uninstrumented ACDF. The BAK/C interbody fusio system consists of square-threaded, hollow, titanium alloy cylind with openings to allow for bone growth through the device.

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